

Remarks

Claim 64 has been canceled without prejudice to the filing of continuing applications. Claims 54-56, 58, 62 and 65 have been amended to more distinctly claim the subject matter that Applicants regard as the invention. No new matter is added with these amendments.

Claims 55-56 and 58 stand rejected under 35 U.S.C. § 112, second paragraph for using the term “non-nucleoside” and “non-nucleotide”. Accordingly, the claims have been amended by deleting the terms “non-nucleoside” and “non-nucleotide” and replacing therefore with “abasic moiety”. Applicants submit that the phrase “abasic moiety” of amended claims 54-56 and 58, along with claim 62, is not vague and indefinite. Specifically, the specification at page 26 defines an “abasic” compound as “a sugar moiety lacking a base or having other chemical groups in place of the base at the 1' position.” Thus, abasic moieties are limited to certain chemical structures, i.e. those with a sugar backbone lacking a base. Withdrawal of the indefinite rejection of claims 55-56, 58 and 62 is respectfully requested.

Next, claim 54 has also been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner contends that the phrase “chemical linkage” is vague and indefinite. The claim has been amended such that it specifically refers to a “succinyl linkage”, the definition of which is well known by those skilled in the art and provided for at page 14, lines 13-16 of the specification. Withdrawal of rejection is respectfully requested.

Moving on, the phrase “terminal chemical group” found in claim 54 has also been found vague and indefinite by the Examiner. Applicants respectfully disagree, as this represents a functional limitation of the claim. To this end, the phrase “terminal chemical group *from which an oligonucleotide can be synthesized*” (emphasis added) must be considered as a whole. One skilled in the art would recognize that only certain chemical moieties could be employed as a scaffold for such oligonucleotide synthesis. For this reason, withdrawal of the rejection is respectfully solicited.

Next, claim 58 has been amended by deleting the phrase “conditions suitable”. Further, the claim has been amended such that it properly depends from claim 54. Withdrawal of the 35 U.S.C. § 112, second paragraph rejection of claim 58 is therefore respectfully requested.

Claims 65-70 have also been rejected under 35 U.S.C. § 112, second paragraph for being indefinite. Specifically, the Examiner contends that the claims contain certain phrases, such as, for example, “said abasic succinate” as found in claim 65, for which there exists no antecedent basis. Applicants respectfully disagree, as the respective claims from which these claims depend from do, indeed, contain these limitations. Turning to claim 65 as an example, the claim depends from claim 62, which in turn depends from claim 55, which in turn depends from claim 54, and thus requires a succinyl linkage (for W) and an abasic moiety (for B) joined as $|-W-B$. It follows that describing W and B under standard IUPAC rules, i.e naming from the outside in, would require it to be the “abasic succinate”. A similar analysis can be applied to claims 66-70. For this reason, withdrawal of the rejection is respectfully requested.

Finally, claims 54-70 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kobayashi in view of Nelson. Kobayashi teaches compounds of the formula $(RO)_3Si(CH_2)_3NH(CH_2)_nNH_2$, wherein R is an alkyl group from 1 to 4 carbons and n is an integer from 5 to 12, and immobilizing such compounds on an inorganic support (at the silane). Nelson teaches a compound $SP-O-Si(OMe)_2(CH_2)_3OCH_2CH(OAc)CH_2OC(O)NH(CH_2)_6NHC(O)(CH_2)_2C(O)OCH(CH_2OD MT)(CH_2NHFMoc)$ ("MF-CPG"), useful in solid phase oligonucleotide synthesis. The Examiner contends it would have been obvious "to use *any chemical entity* from which an oligonucleotide can be synthesized as the physiologically active substance immobilized on an aminoalkylalkoxysilane treated support, as taught by Kobayashi, by including a spacer molecule as suggested by Nelson with a reasonable expectation of success." (emphasis added). Applicants respectfully disagree.

The cited prior art, alone or in combination, simply does not teach or remotely suggest the compounds of the instant claims. Specifically, the claimed compounds are of the formula $SP-O-Si(OCH_3)_2(CH_2)_3NH(CH_2)_6NH-W-B$. These compounds are structurally distinct from the compounds disclosed in Kobayashi or Nelson. Kobayashi teaches N-(6-aminohexyl)-3-aminopropyltrimethoxysilane, and the immobilized compound thereof. Kobayashi further discloses that this immobilized compound "is capable of covalently bonding with physiologically active substances based on the primary amino group." (see column 3, lines 1-4). While the cited prior art patent suggests covalently bonding enzymes, antibodies and antigens to the immobilized N-(6-aminohexyl)-3-aminopropyltrimethoxysilane, the reference simply does not teach or

remotely suggest bonding chemical groups from which an oligonucleotide can be synthesized.

In fact, as noted in the response to the previous office action, the status of the prior art before the instant invention was that the efficiency of oligonucleotide synthesis was influenced by the length and type of spacer, and that the efficiency of DNA synthesis was relatively high so long as the spacer length was at least 24 atoms. (specification at page 3, line 28-page 4, line 18).

The compounds of the present invention comprise spacers 16 atoms in length.¹ As noted in the previous response, the yields are surprisingly as good as those with longer spacers (see FIG 2 and compare with FIG 10). Based on the prior art, one skilled in the art would have not been motivated to combine the teachings of Nelson (see FIG 1 in Nelson, wherein the spacer of the molecule is 24²) with the teachings of Kobayashi because the teachings of the prior art would have *taught away* from such a combination, i.e. the synthesis of an oligonucleotide having a spacer less than 21 atoms long would have been considered to *not* have been efficient. Applicants have surprisingly discovered that the claimed compounds having 16 spacers are synthesized in yields exceeding greater than 80%.

In addition, the spacer of the compound disclosed in Nelson is also a different type, i.e. a different chemical entity. The spacer of the compounds in the instant invention is a succinylaminohexylaminopropylsilate wherein that of the compound taught in Nelson is a succinylaminohexylaminocarboxy-(2-O-actetylpropyl)oxypropylsilate.

¹ In the previous response to office action, Applicants mistakenly counted 12 spacers, forgetting the 4 spacers for the "W" succinyl linkage.

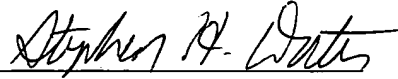
² Applicants note that the Examiner mistakenly counted 18 spacers for MF-CPG in FIG 1 of Nelson. In fact, an oxygen is missing between the support and the Si, and counting up to the oxygen after the succinyl linkage makes 24.

The two spacers have a distinct and separate status in the art and are thus expected by those skilled in the art to have different properties. For the above reasons, withdrawal of the obviousness rejection is respectfully requested.

Allowance of the claims and passage of the case to issue are respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312) 913-0001.

Respectfully submitted,

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